

New brain sensor offers answers about Alzheimer's

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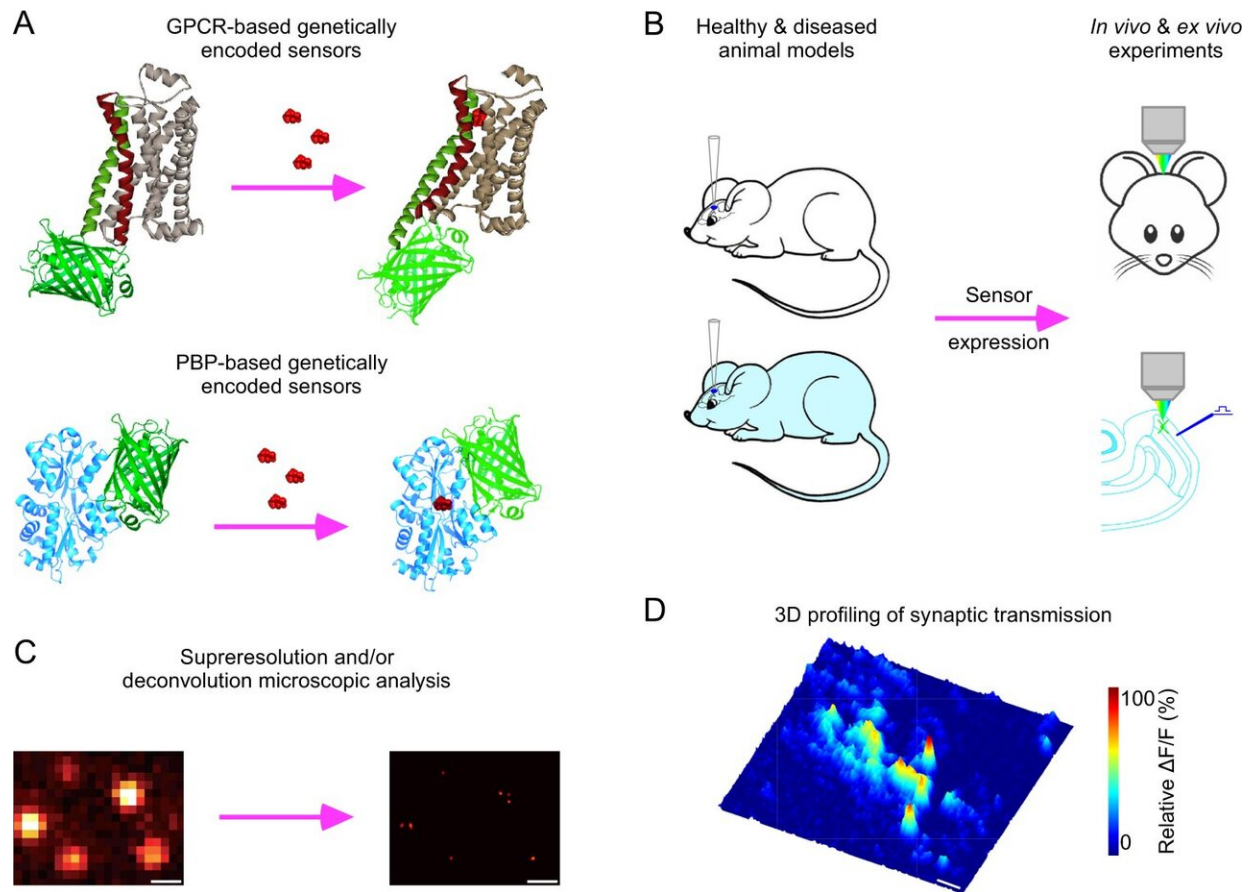


Fig. 1: High-resolution analysis of genetically encoded sensor-illustrated transmission. A Schematic of G protein-coupled receptor (GPCR)- and bacterial periplasmic binding protein (PBP)-based genetically encoded sensors for neuromodulatory transmitters. B Schematic of viral expression, *in vivo* and *ex vivo* applications of genetically encoded sensors. C Schematic of superresolution and/or deconvolution microscopic analysis of image data obtained with genetically encoded sensors. D Three-dimensional spatiotemporal profiling of

synaptic transmission. Note the collection of exemplary animal experimental data made with the recently published project [32]. Credit: *Molecular Psychiatry* (2020). DOI: 10.1038/s41380-020-00960-8

Scientists at the University of Virginia School of Medicine have developed a tool to monitor communications within the brain in a way never before possible, and it has already offered an explanation for why Alzheimer's drugs have limited effectiveness and why patients get much worse after going off of them.

The researchers expect their new method will have tremendous impact on our understanding of depression, [sleep disorders](#), autism, [neurological diseases](#) and major psychiatric conditions. It will speed [scientific research](#) into the workings of the [brain](#), they say, and facilitate the development of new treatments.

"We can now 'see' how [brain cells](#) communicate in sharp detail in both the healthy and diseased brains," said lead researcher J. Julius Zhu of UVA's Department of Pharmacology.

Unexpected Transmissions

The new method developed by Zhu and his collaborators lets scientists examine transmissions inside the brain at both the microscopic level and the far, far smaller nanoscopic level. It combines a biological "sensor" with two different forms of cutting-edge imaging.

The approach can quantify "neuromodulatory" transmissions, which are associated with major brain disorders, including addiction, Alzheimer's, depressive disorders and schizophrenia. They're also linked to autism, epilepsy, eating disorders and sleep disorders.

Neuromodulatory transmissions are the "slower" transmissions in the brain. They're typically thought to involve lots of neurons in large regions. That's in contrast to the much faster transmissions that happen neuron-to-neuron.

But Zhu's new tool has already shown it's not that simple.

In Alzheimer's disease, Zhu and his colleagues discovered a surprising degree of "fine control and precision" in the supposedly shotgun neuromodulatory transmissions. Widely used Alzheimer's drugs known as [acetylcholinesterase inhibitors](#) may inhibit this precise communication, the scientists report. That may explain the limited effectiveness of the drugs, they say.

The researchers went on to identify potential changes in the brain that could be brought about by long-term use of the drugs, which could explain why patients often get much worse when they stop taking them. "The new method points out Alzheimer's defects in the unprecedented spatial and temporal resolution, defining the precise targets for medicine," Zhu said.

Alzheimer's, the researchers say, is just the tip of the iceberg. The new system has "broad applicability" across the spectrum of neurological and psychiatric diseases and disorders, they report in two new scientific papers. In the years to come, the scientists predict, it will help doctors understand neurological illnesses and [psychiatric problems](#), screen drugs for potential treatments, identify disease-causing genes and develop better, more personalized medicine tailored for specific patient needs.

"If we see problems," Zhu said, "we will be ready to treat them."

The researchers have described new approach and their findings in the scientific journals *Molecular Psychiatry* and *Nano Letters*.

More information: Li Lin et al. Genetically encoded sensors enable micro- and nano-scopic decoding of transmission in healthy and diseased brains, *Molecular Psychiatry* (2020). [DOI: 10.1038/s41380-020-00960-8](https://doi.org/10.1038/s41380-020-00960-8)

Paula K. Zhu et al. Nanoscopic Visualization of Restricted Nonvolume Cholinergic and Monoaminergic Transmission with Genetically Encoded Sensors, *Nano Letters* (2020). [DOI: 10.1021/acs.nanolett.9b04877](https://doi.org/10.1021/acs.nanolett.9b04877)

Provided by University of Virginia

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